REMARKS/ARGUMENTS

With this amendment, claims 1, 6, 14-16, 19, 28 and 29 are pending. New claims 30 and 31 are added. For convenience, the Examiner's rejections are addressed in the order presented in the January 24, 2005 Office Action.

Rejections under 35 U.S.C. §112, first paragraph, enablement

Claims 1, 6, 14-15, 19, 28 and 29 are rejected under 35 U.S.C. §112, first paragraph because allegedly, the specification does not provide enablement for one of skill to make and use an invention commensurate in scope with those claims, *i.e.*, methods to use an ILKAP protein with 90% identity to SEQ ID NO:2. The Office Action also alleges that undue experimentation is required to practice the claimed invention. It is the Applicants' understanding that new claim 31 is allowable. To the extent the rejection applies to the claims as amended, Applicants respectfully traverse the rejection.

Factors such as the amount of guidance presented in the specification and the presence of working examples must be considered to determine whether undue experimentation is required to practice the claimed invention. *See, e.g.*, *Ex Parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int. 1985) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). As described in *Wands*, "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *Wands*, USPQ2d at 1404, quoting *In re Jackson*, 217 USPQ 804 (Bd. Pat. App. & Int. 1982). Moreover, "[a] patent need not teach, and preferably omits, what is well known in the art." MPEP 2164.01 *citing In re Buchner*, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 221 USPQ 481, 489 (Fed. Cir. 1984).

As set forth in the Manual of Patent Examining Procedure (MPEP) § 2164.01, "the test of enablement is not whether any experimentation is necessary, but whether... it is undue." Further, the "fact that experimentation may be complex does not necessarily make it

undue, if the art typically engages in such experimentation" (citations omitted). Finally, claims reading on inoperative embodiments are enabled if the skilled artisan understands how to avoid inoperative embodiments. *See, e.g., In re Cook and Merigold*, 169 USPQ 299, 301 (C.C.P.A. 1971).

The current Office Action alleges that an "excessive and undue" amount of experimentation is required by those of skill to practice the claimed invention. Office Action at a page 3. The Office Action reasons that the specification does not enable one of skill to predictably determine changes to the ILKAP protein that can tolerated and still fall within the claims and therefore that undue experimentation is required to practice the claimed invention. In response, Applicants provide as Exhibit A, a declaration from Dr. Sacha Holland demonstrating that based on the disclosure of the specification and the knowledge of those of skill at the time of filing, identification of functional ILKAP polypeptides with 90% identity to SEQ ID NO:2 was routine at the time of filing and that undue experimentation is not required by those of skill to practice the claimed invention.

Dr. Holland first discusses a reference that demonstrates that the ILKAP protein has serine/threonine phosphatase activity and that discloses conserved amino acid residues in the ILKAP amino acid sequence based on sequence alignments with protein phosphatase 2C (PP2C) family members. *See, e.g.*, Leung-Hagesteijn *et al.*, *EMBO J.*, 20:2160-2170 (2001) cited in specification at page 3, lines 25-28; page 45, lines 2-3 and 15-17 and submitted as Exhibit B. Dr. Holland also discusses the angiogenesis activity of ILKAP that was experimentally determined and disclosed in the specification at Example 1. Dr. Holland points out that the structure of members of the PP2C family had been determined before the filing date. *See, e.g.*, Das *et al.*, *EMBO J.* 15:6798-6809 (1996), submitted as Exhibit C. Dr. Holland asserts that the ILKAP protein shows a high degree of alignment with conserved data base domain that are based on PP2C family members. *See, e.g.*, alignments of Exhibit D. Dr. Holland states that those of skill would recognize conserved amino acids residues based on the alignment of Das *et al.* and Exhibit D. Dr. Holland also states that those of skill would recognize that modification of the conserved amino acid residues would be most likely to have a detrimental effect on protein

activity. Dr. Holland also states that generation of ILKAP proteins that have 90%identity to SEQ ID NO:2 is routine and within the capabilities of those o skill without undue experimentation.

Dr. Holland reviews the assays that are available to those of skill in order to determine whether an ILKAP protein with 90% identity to SEQ ID NO:2 is functional. According to Dr. Holland the functional assays are routine and could be done by a skilled laboratory technician. In addition, many of the assays are amenable to high throughput methods. Therefore, according to Dr. Holland, identification of functional ILKAP proteins that have 90%identity to SEQ ID NO:2 is routine and within the capabilities of those o skill without undue experimentation.

The Office Action cited three references, as supporting the rejection for alleged lack of enablement, *e.g.*, Atwood (2000), Skolnick and Fetrow (2000), and Metzler *et al.* (1997). Dr. Holland reviewed the references and disagrees with the analysis of the Office Action. According to Dr. Holland, the Atwood and Skolnick references do not apply to claimed ILKAP protein because its function has been experimentally determined and that Metzler *et al.* demonstrates that the effects of modification of amino acid residues can be predicted in advance, especially when sequence alignments are used to identify conserved amino acid residues.

Dr. Holland asserts that certain techniques that are well known in the art can by used by those of skill to routinely identify and, if necessary, to routinely generate proteins that have 90% identity to SEQ ID NO:2. Those techniques include determination of percent identity between amino acid sequences and cloning techniques, such as PCR based mutagenesis. Dr. Holland also asserts that the specification provides disclosure of angiogenesis assays that can be routinely done by those of skill to identify functional ILKAP proteins.

The Office Action at page 2 appears to assert that the term "identity is not defined in the application. Applicants respond by pointing to a definition of identity in the specification at page 7, page 25, through page 9, line 21. The definition includes, *e.g.*, references to algorithms used to determine percent identity between two sequences.

Based on the knowledge of these techniques in the art or their disclosure in the specification, those of skill would understand how to avoid inoperative embodiments. Applicants respectfully remind the Examiner that routine screening for operative embodiments is not precluded by the statute. For example, in *In re Wands*, the Federal Circuit agreed that screening is appropriate in technologies that do so routinely to identify embodiments with desired characteristics. *See, e.g., In re Wands*, 8 USPQ2d 1400, 1406-7 (Fed. Cir. 1988). Here, those of skill routinely assay ILKAP proteins for angiogenesis activity, whether the ILKAP proteins are engineered or naturally occurring.

In order to establish a prima facie case of lack of enablement, the Examiner has the burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). The Examiner has not provided any reason why those of skill would not be able to identify proteins with 90% identity to SEQ ID NO:2 and angiogenesis activity based on the disclosure of the specification and the knowledge of the art at the time of filing. Applicants respectfully assert that based on the disclosure of the specification and the state of the art at the time of filing, the claimed proteins are enabled.

Applicants respectfully bring to the Examiner's attention a recent decision by the Board of Patent Appeals and Interferences: *Ex parte Sun*, Appeal No. 2003-1993. In *Sun*, the board found that claims directed to sequences with 80% identity to a reference sequence were enabled because the supporting specifications provided a single reference sequence and an assay for activity of the encoded protein. Again, Applicants respectfully assert that based on the disclosure of the specification and the state of the art at the time of filing, the claimed proteins are enabled.

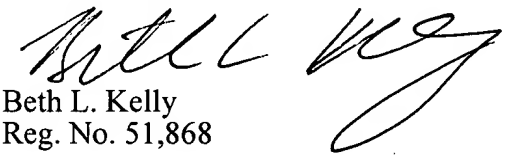
In view of the above arguments, withdrawal of the rejections for alleged lack of enablement is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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